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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/942,498	08/30/2001	Jennifer E. Van Eyk	PTQ-0038	9446

7590 10/22/2002

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EXAMINER
DAVIS, RUTH A

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 10/22/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/942,498	EYK ET AL.	
	Examiner	Art Unit	
	Ruth A. Davis	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *4-11,13 and 15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,12,14,16-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1–3, 12 and 14 in Paper No. 8 is acknowledged. The traversal is on the ground(s) that the inventions of groups II and III are related and dependent upon one another, that the methods are all related due to the discovery that MLC1 phosphorylation is linked with protecting cardiovascular muscles and that the searches must overlap, requiring no undue burden on examiner. This is not found persuasive because as stated in the previous office action, other materially different products could be used in a method to protect cardiac and skeletal muscles from damage such as milk thistle (from viral damage). Also, while the search for one group may overlap another, applicant is reminded that an overlapping search is not a coextensive search. Furthermore, the separate classification of each group further supports establishment of a serious undue burden on examiner.

The requirement is still deemed proper and is therefore made FINAL.

Applicant's amendment has been received and entered into the case. Claims 16–21 have been added and drawn to elected subject matter. Therefore, claims 1–3, 12, 14 and 16–21 have been considered on the merits. Claims 4–11, 13 and 15 have been withdrawn from consideration as being drawn to non-elected subject matter.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1–3, 12, 14 and 16–21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 and its dependents are drawn to a method for identifying a muscle protective agent however are rendered vague and indefinite because the claims fail to set forth any positive limitations regarding how one would determine if the agent is in fact a muscle protecting agent. For example, after assessing the ability of a potential agent to increase MLC1 phosphorylation, it is unclear what result indicates the agent is a muscle protective agent. (i.e. Does the ability of increasing phosphorylation alone, indicate a protective agent?)

The claims are rendered vague and indefinite for reciting "muscle protective agent" because this term is not adequately defined by the claim language or specification. It is unclear what is included or excluded by the term, thereby failing to distinctly claim what applicant regards as claimed subject matter.

Claim 1 and its dependents are further indefinite for reciting MLC1 without first writing out the full term followed by the abbreviation in parenthesis.

Claim 2 is confusing for reciting "or" in lines 4 and 5 because it is unclear which terms are intended to be in the alternative.

Claim 12 is drawn to a method for identifying new therapeutic targets as muscle protective agents however are rendered vague and indefinite because the claim fails to set forth

any positive limitations regarding how one would determine if the agent is in fact a therapeutic target or muscle protecting agent. For example, after identifying that a kinase or phosphatase acts on MLC1 phosphorylation, it is unclear what result indicates the agent is a target/muscle protective agent. (i.e. Does the ability to act on phosphorylation alone, indicate a protective agent?) Furthermore, it is unclear if the kinase and/or phophatase is the identified therapeutic target, once it is determined to act on MCL1 phosphorylation.

Claim 12 is further indefinite because it is unclear what constitutes "acting on MCL1 phosphorylation". For example, how does the target "act on" MLC1 phosphorylation? Does the target increase, decrease or inhibit phosphorylation? Is it unimportant as to how a therapeutic targets acts on MLC1 phosphorylation?

Claim 14 is rendered vague and confusing for reciting "IN sequence extraction" because the phrase is not adequately defined by the claim language or specification.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1–3, 12, 14 and 16–21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kaibuchi et al. (US 5906819).

Applicant claims a method for identifying a muscle protective agent, the method comprising assessing the ability of a potential protective agent to increase MLC1 phosphorylation. The ability of the potential agent to increase MLC1 phophorylation is assessed in vitro in purified myosin, purified myosin light chain 1, purified isoforms of myosin light chain 1, or in myofilament or skinned muscle fibers and the myosin, myosin light chain 1 or isoforms thereof are obtained from a biological sample using IN sequence extraction. Alternatively, the agent is assessed in isolated myocytes or whole hearts that are isolated or in vivo. Specifically, MLC1 phosphorylation is increased by modulation of a phosphatase or kinase that acts on MLC1 phosphorylation and occurs at one or more residues Thr64, Ser194 or Ser195 of human MLC1 or one or more residues Thr69 or Ser200 of rat MLC1. The protective agent identified protects against muscle damage caused by cardiomyopathies, hypertension, or free radicals or alternatively damage caused by ischemia, hypoxia, or ischemia/hypoxia with reperfusion. Applicant additionally claims a method for identifying new therapeutic targets as muscle protective agents, the method comprising identifying kinases or phosphatases that act on MLC1 phosphorylation.

Kaibuchi et al. teaches methods for screening (identifying) materials (or muscle protective agents) that inhibit Rho kinase activity (col.4 line 50-55). Suitable substrates for assessing the inhibition activity include muscle cells (myocytes) (col.17 line 27-33), myosin and MLC (col.18 line 27-33). Kaibuchi also teaches that Rho kinase phosphorylates MLC in cells and isolated MLC, wherein the primary site of phosphorylation is on Ser and Thr (col.15 line 35-40, example 8). Kaibuchi teaches that the identified agents which inhibit Rho kinase can be used to treat various circulatory system diseases such as hypertension, cardiac angina (leading to ischemia or hypoxia) or myocardial infarction (col.16 line 2-8).

Since Rho kinase is disclosed to increase MLC phosphorylation (col.15 line 62-63), identifying the ability of an agent to inhibit Rho kinase activity effectively assesses the ability of that agent to increase (or act one) MLC1 phosphorylation. In addition, myosin light chain phosphatase is disclosed to be a most suitable substrate for Rho kinase (col.15 line 24-30), which may effectively modulates Rho kinase, in turn modulating (increasing) MLC phosphorylation.

Kaibuchi does not teach the method wherein MLC is obtained from a biological sample using IN sequence extraction. However, the method of producing or obtaining MLC does not appear to structurally alter the MLC. As such the claimed MLC reasonably appears to be identical with that disclosed in the reference.

Kaibuchi does not teach the specific residues at which phosphorylation occurs. However, at the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to expect increased phosphorylation on the claimed residues, since Kaibuchi specifically teaches that Ser and Thr are the primary sites of phosphorylation. Furthermore, location of such activity is inherent to the disclosed methods, since the method steps are the same.

Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated to practice the methods of Kaibuchi with a reasonable expectation for identifying muscle protective agents.

7. Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over De Lanorelle (WO 97/26268).

Applicant claims a method for identifying a muscle protective agent, the method comprising assessing the ability of a potential protective agent to increase MLC1 phosphorylation.

De Lanorelle teaches processes for inhibiting cell proliferation and motility by increasing the phosphorylation of myosin light chain in the cell (p.1 line 2-6). The abnormal growth of smooth muscle cells restricts blood flow and is known as intimal hyperplasia (p.1 line 8-10). De Lanorelle teaches that inhibiting cell proliferation (or protecting the muscle) is achieved by increasing phosphorylation of MLC via MLC kinase in a cell (p.2 line 22-27). Moreover, De Lanorelle teaches that by increasing MLC phosphorylation in cells, muscle cells are protected.

De Lanorelle does not teach a method for identifying a muscle protective agent by assessing the ability of an agent to increase MLC1 phosphorylation. However, at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to do so since De Lanorelle specifically teaches that increased MLC phosphorylation protects muscle cells from damage. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by De Lanorelle to reasonably expect agents which increase MLC phosphorylation to also be muscle protective agents.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruth A. Davis whose telephone number is 703-308-6310. The examiner can normally be reached on M-H (7:00-4:30); altn. F (7:00-3:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 703-308-0196. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Ruth A. Davis; rad
October 18, 2002

LEON B. LANKFORD, JR.
PRIMARY EXAMINER

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